

Reference: 5

CONFIDENTIAL

IFO 26/27/851445

ITF 282

ONE YEAR ORAL

TOXICITY STUDY IN RATS

VOL 5

CONFIDENTIAL

Addressee:

Professor G. Sportoletti,
Italfarmaco Spa,
20126 Milano,
Viale Fulvio Testi 330,
ITALY.

14 March 1986.

Authors:

L. E. Fish,
D. J. Lewis,
C. Gopinath.

Huntingdon Research Centre Ltd.,
Huntingdon,
Cambridgeshire,
PE18 6ES,
ENGLAND.

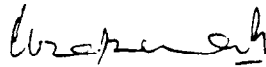
We the undersigned, hereby declare that the work was performed under our supervision according to the procedures herein described, and that this report provides a correct and faithful record of the results obtained.



L. Elizabeth Fish, B.V.M.S., M.R.C.V.S.,
Pathologist



David J. Lewis, B.Sc., Ph.D., M.I.Biol., M.R.C.Path.,
Deputy Head - Department of Pathology



Chirukandath Gopinath, B.V.Sc., M.V.Sc., Ph.D., M.R.C.Path.,
Director of Pathology

QUALITY ASSURANCE AUDIT STATEMENT

HRC REPORT No. IFO 26/27/851445

This histopathology report has been audited by HRC Quality Assurance Unit. It is considered to be an accurate presentation of the findings.

PR:ll

Peter H.C.V. Richold, B.Sc.,
Systems Compliance Auditor.

12 3 86

Audit notes

Data are verified by means of sampling methods as described in British Standards Institution BS 6000, 6001 (1972) and US Military Standard 105D, the Acceptable Quality Level (the maximum percentage errors considered satisfactory as a process average) being 0.4.

Any computerised presentations which are the outcome of verified

CONTENTS

IFO/26/27

Page

MATERIALS AND METHODS

1

RESULTS

Changes related to experimental procedure
Incidental findings

2
2

TABLE

Microscopic pathology incidence summary

3 - 10

APPENDIX

Rats killed at termination

11 - 117

Prepared slides stained with haematoxylin and eosin or by Perls' Prussian blue method for iron together with further tissues embedded in paraffin wax were received from Italfarmaco S.p.a. Milan. The material was from Wistar rats dosed with the test compound, ITF 282, daily for 52 weeks, by oral gavage.

Histopathological examination was performed on male and female rats from control and 85 mg/kg/day ITF 282 groups killed at termination of the study.

Slides were received, stained with haematoxylin and eosin, of the following tissues:

liver	duodenum
spleen	ileum
kidney	jejunum
	caecum
	colon

Additional sections stained by Perls' Prussian blue method for iron were received of the following tissues:

liver	spleen
-------	--------

Paraffin wax blocks were received of samples of the following tissues:

heart	cervical lymph nodes
aorta	(usually salivary gland)
salivary glands	adrenals
lungs	pancreas
thyroids	urinary bladder
trachea	seminal vesicles
brain	stomach
pituitary	Oesophagus
testes	spinal cord
ovaries	muscle
uterus	eyes
prostate	sternum

These tissues were sectioned (at HRC) at 5 μ m and stained with haematoxylin and eosin.

Additional sections of lung from a proportion of rats were stained by Perls's Prussian blue method for iron.

Individual animal histopathological findings are given in the Appendix and group lesion incidences summarised in the tables. The following comments are made in summary:

No treatment-related changes were detected.

CHANGES RELATED TO EXPERIMENTAL PROCEDURE

Minimal foci of pigmented macrophages were observed in the lungs in 3/23 male and 5/29 female rats receiving 85 mg/kg/day ITF 282 as compared with 1/32 female rats and none in male rats in the control group. Moderate foci of pigmented macrophages were recorded in 5/23 male rats and 6/29 female rats in the 85 mg/kg/day group but not in any control animals. In addition one male rat receiving 85 mg/kg/day had a single focus of pigmented macrophages.

A proportion of lung sections from these rats was stained by Perls' Prussian blue method and the pigment stained positively indicating haemosiderin.

In view of the nature of the compound and in the absence of systemic effects the most likely explanation for this pulmonary haemosiderosis is incorrect dosing during oral gavage with introduction of test compound into the lungs.

INCIDENTAL FINDINGS

Other lesions described in the individual animal reports and listed in the tables were considered spontaneous in origin and therefore of no toxicological significance.

IFO/26/27

Microscopic pathology incidence summary

[illegible]

TABLE

IFO/26/27

(Pathology - continued)

	Males					Females				
	0	1	2	3	4	0	1	2	3	4
Animals Logged:	22	0	0	0	23	32	0	0	0	29
Marked peribronchiolar lymphoid aggregates . . .	0	0	0	0	1	1	0	0	0	0
Minimal peribronchiolar acini with inflammation	1	0	0	0	8	6	0	0	0	8
Moderate peribronchiolar acini with inflammation	1	0	0	0	4	2	0	0	0	3
Bronchiectasis	0	0	0	0	2	2	0	0	0	1
Minimal focal pneumonitis	1	0	0	0	0	0	0	0	0	0
Focal pneumonitis	1	0	0	0	0	0	0	0	0	0
Minimal pneumonitis	8	0	0	0	11	16	0	0	0	15
Moderate pneumonitis	0	0	0	0	4	3	0	0	0	4
Focal purulent bronchopneumonia	0	0	0	0	1	0	0	0	0	0
Purulent bronchopneumonia	1	0	0	0	1	0	0	0	0	0
Bronchopneumonia	0	0	0	0	0	5	0	0	0	2
Pulmonary abscess(es)	0	0	0	0	2	1	0	0	0	0
Moderate perivascular mononuclear cells	1	0	0	0	0	0	0	0	0	0
Moderate alveolar congestion/haemorrhage	1	0	0	0	0	0	0	0	0	0
Foci of alveolar haemorrhage	0	0	0	0	1	0	0	0	0	1
Focal alveolar haemorrhage	0	0	0	0	1	1	0	0	0	0
Moderate alveolar haemorrhage	0	0	0	0	0	0	0	0	0	2
Minimal alveolar oedema	0	0	0	0	0	0	0	0	0	1
Bronchiolar haemorrhage	0	0	0	0	1	0	0	0	0	0
Blood in bronchioles	0	0	0	0	0	1	0	0	0	0
Foci of alveolar macrophages	1	0	0	0	0	0	0	0	0	0
Focus of foamy macrophages	0	0	0	0	0	0	0	0	0	1
Minimal foci of foamy macrophages	0	0	0	0	0	1	0	0	0	0
Moderate foci of foamy macrophages	0	0	0	0	2	0	0	0	0	0
Areas of foamy macrophages	0	0	0	0	1	0	0	0	0	0
Granuloma with central mineralisation	0	0	0	0	1	0	0	0	0	0
Minimal foci of mineralisation	0	0	0	0	1	0	0	0	0	0
Pulmonary cyst not visible in sections provided	1	0	0	0	0	0	0	0	0	0
Cyst not present in sections examined	0	0	0	0	0	0	0	0	0	1
Lymph nodes	22	0	0	0	23	32	0	0	0	29
Not Remarkable	2	0	0	0	1	5	0	0	0	2
Missing	20	0	0	0	22	27	0	0	0	26
Abscess	0	0	0	0	0	0	0	0	0	1
Liver	22	0	0	0	23	32	0	0	0	29
Not Remarkable	11	0	0	0	11	28	0	0	0	17
Missing	0	0	0	0	1	2	0	0	0	4
Minimal foci of mononuclear cells	4	0	0	0	4	2	0	0	0	5
Minimal periportal mononuclear cells	1	0	0	0	0	0	0	0	0	0
Minimal bile duct hyperplasia	0	0	0	0	0	0	0	0	0	1
Focal bile duct proliferation	2	0	0	0	0	0	0	0	0	0
Focus of ground glass hepatocytes	0	0	0	0	1	0	0	0	0	0
Minimal foci of ground glass hepatocytes	3	0	0	0	1	0	0	0	0	0

TABLE

IFO/26/27

(Pathology - continued)

	Males					Females				
	0	1	2	3	4	0	1	2	3	4
Animals Logged:	22	0	0	0	23	32	0	0	0	29
Minimal foci of basophilic hepatocytes	0	0	0	0	1	0	0	0	0	0
Focus of hypertrophic hepatocytes	0	0	0	0	0	0	0	0	0	1
Minimal foci of hypertrophic hepatocytes	1	0	0	0	2	0	0	0	0	0
Minimal foci of siderocytes	1	0	0	0	0	0	0	0	0	0
Area of fibrosis and siderocytes	1	0	0	0	0	0	0	0	0	0
Area of fibrosis, inflammation and adipose tissue	1	0	0	0	0	0	0	0	0	0
Area of mineralisation fibrosis and inflammation	1	0	0	0	0	0	0	0	0	0
Focal periportal fibrous tissue scarring	1	0	0	0	0	0	0	0	0	0
Early fibrous bridging	0	0	0	0	0	0	0	0	0	1
Focal hepatocyte necrosis	0	0	0	0	0	0	0	0	0	1
Minimal foci of hepatocyte vacuolation	0	0	0	0	1	0	0	0	0	0
Minimal vacuolated hepatocytes	0	0	0	0	0	0	0	0	0	3
Focus of vacuolated hepatocytes	0	0	0	0	1	0	0	0	0	0
Granuloma with central mineralisation	0	0	0	0	1	0	0	0	0	0
Liver Perls'	22	0	0	0	23	32	0	0	0	29
Not Remarkable	22	0	0	0	20	8	0	0	0	9
Missing	0	0	0	0	1	1	0	0	0	4
Trace of Perls' positive material	0	0	0	0	1	0	0	0	0	0
Minimal Perls' positive material	0	0	0	0	1	0	0	0	0	0
Trace of centrilobular Perls' positive material	0	0	0	0	0	21	0	0	0	16
Minimal centrilobular Perls' positive material	0	0	0	0	0	2	0	0	0	0
Spleen	22	0	0	0	23	32	0	0	0	29
Not Remarkable	21	0	0	0	21	29	0	0	0	26
Missing	0	0	0	0	0	1	0	0	0	2
Minimal extramedullary haemopoiesis	1	0	0	0	2	2	0	0	0	1
Spleen Perls'	22	0	0	0	23	32	0	0	0	29
Not Remarkable	0	0	0	0	0	0	0	0	0	0
Missing	0	0	0	0	1	1	0	0	0	2
Trace of Perls' positive material	1	0	0	0	1	0	0	0	0	1
Minimal Perls' positive material	15	0	0	0	11	0	0	0	0	0
Moderate Perls' positive material	6	0	0	0	10	25	0	0	0	24
Marked Perls' positive material	0	0	0	0	0	6	0	0	0	2
Pancreas	22	0	0	0	23	32	0	0	0	29
Not Remarkable	16	0	0	0	16	25	0	0	0	16
Missing	2	0	0	0	4	2	0	0	0	7
Minimal peri-islet siderocytes	1	0	0	0	0	0	0	0	0	0
Minimal periarteritis	1	0	0	0	0	0	0	0	0	0
Minimal focal inflammation	0	0	0	0	1	0	0	0	0	0
Exocrine acinar atrophy	2	0	0	0	2	5	0	0	0	6

TABLE

IFO/26/27

(Pathology - continued)

	Males					Females				
	0	1	2	3	4	0	1	2	3	4
Animals Logged:	22	0	0	0	23	32	0	0	0	29
Kidneys	22	0	0	0	23	32	0	0	0	29
Not Remarkable	11	0	0	0	5	22	0	0	0	16
Missing	0	0	0	0	0	1	0	0	0	0
Minimal foci of interstitial mononuclear cells	7	0	0	0	14	2	0	0	0	6
Moderate foci of interstitial mononuclear cells	1	0	0	0	1	0	0	0	0	1
Focus of basophilic cortical tubules	2	0	0	0	1	0	0	0	0	0
Minimal foci of basophilic cortical tubules	7	0	0	0	4	0	0	0	0	0
Moderate foci of basophilic cortical tubules	0	0	0	0	1	0	0	0	0	0
Focus of dilated cortical tubules with eosinophilic contents	0	0	0	0	0	0	0	0	0	2
Occasional dilated tubules with eosinophilic contents	1	0	0	0	0	0	0	0	0	0
Foci of dilated cortical tubules with eosinophilic contents	0	0	0	0	1	0	0	0	0	0
Minimal foci of dilated cortical tubules with eosinophilic contents	0	0	0	0	1	3	0	0	0	3
Minimal progressive glomerulonephrosis	0	0	0	0	0	4	0	0	0	2
Cortical cyst	1	0	0	0	0	0	0	0	0	0
Peripelvic lymphoid aggregates	0	0	0	0	0	0	0	0	0	1
Minimal inflammation in mesentery	0	0	0	0	1	0	0	0	0	0
Urinary bladder	22	0	0	0	23	32	0	0	0	29
Not Remarkable	15	0	0	0	11	25	0	0	0	17
Missing	2	0	0	0	4	2	0	0	0	7
Parasite(s) in lumen	4	0	0	0	6	5	0	0	0	3
Parasites in mucosa	2	0	0	0	0	4	0	0	0	4
Minimal submucosal mononuclear cells	0	0	0	0	1	0	0	0	0	0
Contains colloid	0	0	0	0	2	0	0	0	0	0
Minimal serosal inflammation	0	0	0	0	1	0	0	0	0	0
Uterus	0	0	0	0	0	32	0	0	0	29
Not Remarkable	0	0	0	0	0	26	0	0	0	16
Missing	0	0	0	0	0	1	0	0	0	5
Endometrial polyp	0	0	0	0	0	1	0	0	0	0
Minimal squamous metaplasia of endometrial glands	0	0	0	0	0	2	0	0	0	0
Minimal dilatation of endometrial glands	0	0	0	0	0	1	0	0	0	2
Minimal dilatation of lumen	0	0	0	0	0	0	0	0	0	5
Moderate dilatation of lumen	0	0	0	0	0	1	0	0	0	1

TABLE

IFO/26/27

(Pathology - continued)

	Males					Females				
	0	1	2	3	4	0	1	2	3	4
Animals Logged:	22	0	0	0	23	32	0	0	0	29
Pituitary	22	0	0	0	23	32	0	0	0	29
Not Remarkable	13	0	0	0	14	25	0	0	0	21
Missing	7	0	0	0	7	4	0	0	0	7
Cyst(s) in pars anterior	2	0	0	0	0	0	0	0	0	0
Focal hyperplasia in pars anterior	0	0	0	0	0	1	0	0	0	0
Adenoma of pars anterior	0	0	0	0	1	1	0	0	0	1
Prominent acini and ducts in pars nervosa	0	0	0	0	1	0	0	0	0	0
Adjacent haemorrhage	0	0	0	0	0	1	0	0	0	0
Salivary gland	22	0	0	0	23	32	0	0	0	29
Not Remarkable	18	0	0	0	19	31	0	0	0	23
Missing	2	0	0	0	3	1	0	0	0	5
Minimal foci of interstitial mononuclear cells	1	0	0	0	0	0	0	0	0	0
Moderate foci of interstitial mononuclear cells	1	0	0	0	0	0	0	0	0	0
Minimal acini atrophy	0	0	0	0	1	0	0	0	0	0
Minimal focal acinar atrophy	0	0	0	0	0	0	0	0	0	1
Oesophagus	22	0	0	0	23	32	0	0	0	29
Not Remarkable	17	0	0	0	20	30	0	0	0	23
Missing	5	0	0	0	3	2	0	0	0	6
Stomach	22	0	0	0	23	32	0	0	0	29
Not Remarkable	13	0	0	0	13	25	0	0	0	17
Missing	2	0	0	0	3	1	0	0	0	0
Minimal mucosal inflammation(g)	3	0	0	0	2	1	0	0	0	0
Minimal submucosal inflammation(g)	4	0	0	0	4	0	0	0	0	0
Minimal submucosal oedema(g)	2	0	0	0	0	0	0	0	0	0
Focal submucosal adipose tissue(g)	1	0	0	0	2	5	0	0	0	12
Ectopic squamous epithelium(g)	0	0	0	0	1	0	0	0	0	0
Minimal submucosal congestion(g)	0	0	0	0	0	0	0	0	0	1
Duodenum	22	0	0	0	23	32	0	0	0	29
Not Remarkable	17	0	0	0	20	28	0	0	0	25
Missing	2	0	0	0	1	4	0	0	0	4
Minimal mucosal inflammation	3	0	0	0	2	0	0	0	0	0
Jejunum	22	0	0	0	23	32	0	0	0	29
Not Remarkable	16	0	0	0	19	27	0	0	0	25
Missing	3	0	0	0	2	3	0	0	0	4
Minimal mucosal inflammation	2	0	0	0	2	0	0	0	0	0
Submucosal lymphoid hyperplasia	1	0	0	0	0	2	0	0	0	0

TABLE
(Pathology - continued)

IFO/26/27

	Males					Females				
	0	1	2	3	4	0	1	2	3	4
Animals Logged.	22	0	0	0	23	32	0	0	0	29
Ileum	22	0	0	0	23	32	0	0	0	29
Not Remarkable	18	0	0	0	16	27	0	0	0	23
Missing.	2	0	0	0	4	3	0	0	0	4
Minimal mucosal inflammation	2	0	0	0	2	0	0	0	0	0
Minimal lymphoid hyperplasia	0	0	0	0	1	2	0	0	0	2
Fat necrosis in mesentery	0	0	0	0	0	0	0	0	0	1
Caecum	22	0	0	0	23	32	0	0	0	29
Not Remarkable	10	0	0	0	15	16	0	0	0	13
Missing.	9	0	0	0	8	10	0	0	0	8
Parasite(s) in lumen	2	0	0	0	0	2	0	0	0	1
Minimal mucosal inflammation	1	0	0	0	0	0	0	0	0	1
Minimal submucosal inflammation	0	0	0	0	0	0	0	0	0	1
Minimal submucosal oedema	0	0	0	0	0	0	0	0	0	1
Minimal submucosal lymphoid hyperplasia	1	0	0	0	0	5	0	0	0	7
Colon	22	0	0	0	23	32	0	0	0	29
Not Remarkable	15	0	0	0	14	20	0	0	0	19
Missing.	2	0	0	0	2	3	0	0	0	3
Parasite(s) in lumen	1	0	0	0	2	5	0	0	0	2
Minimal mucosal inflammation	2	0	0	0	2	0	0	0	0	1
Minimal submucosal inflammation	0	0	0	0	1	0	0	0	0	1
Minimal submucosal lymphoid hyperplasia	2	0	0	0	2	4	0	0	0	4
Skeletal muscle	22	0	0	0	23	32	0	0	0	29
Not Remarkable	12	0	0	0	19	31	0	0	0	23
Missing.	10	0	0	0	4	1	0	0	0	6
Eyes	22	0	0	0	23	32	0	0	0	29
Not Remarkable	18	0	0	0	18	16	0	0	0	17
Missing.	4	0	0	0	4	15	0	0	0	12
Area of retinal atrophy	0	0	0	0	1	0	0	0	0	0
Unilateral retinal atrophy	0	0	0	0	0	1	0	0	0	0
Spinal cord	22	0	0	0	23	32	0	0	0	29
Not Remarkable	12	0	0	0	15	26	0	0	0	20
Missing.	10	0	0	0	8	6	0	0	0	9
Brain	22	0	0	0	23	32	0	0	0	29
Not Remarkable	18	0	0	0	20	28	0	0	0	23
Missing.	4	0	0	0	3	4	0	0	0	6

IFO/26/27

(Pathology - continued)

[illegible]

APPENDIX

IFO/26/27

Rats killed at termination

Group :	0	1	2	3	4
Compound:	-			ITF 282	
Level (mg/kg/day):	Control	10,6	21,2	42,5	85

Histopathological findings are presented by an automated data collection system and the following comments should be noted:

The following abbreviations are used:

n.g.	-	non-glandular (region of stomach)
g	-	glandular (region of stomach)

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 2 /M

Designated: TERMINAL

The following observations were noted:

Aorta	(Missing)
Trachea	(Missing)
Heart	(Missing)
Lungs	(Missing)
Lymph nodes	(Missing)
Liver	Area of fibrosis and siderocytes. Focal bile duct proliferation.
Spleen Perls'	Moderate Perls' positive material.
Pancreas	(Missing)
Kidneys	Minimal foci of interstitial mononuclear cells.
	Minimal foci of basophilic cortical tubules.
Urinary bladder	(Missing)
Prostate	(Missing)
Seminal vesicles	(Missing)
Testes	(Missing)
Thyroids	(Missing)
Adrenals	(Missing)
Pituitary	(Missing)
Salivary gland	(Missing)
Oesophagus	(Missing)
Stomach	(Missing)
Caecum	(Missing)
Skeletal muscle	(Missing)
Eyes	(Missing)
Spinal cord	(Missing)
Brain	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Liver Perls', Spleen, Duodenum, Jejunum, Ileum, Colon.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 3 /M

Designated: TERMINAL

The following observations were noted:

Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Moderate peribronchiolar acini with inflammation. Minimal pneumonitis. Pulmonary cyst not visible in sections provided.
Lymph nodes	(Missing)
Spleen Perls'	Minimal Perls' positive material.
Testes	Moderate unilateral tubular atrophy.
Pituitary	(Missing)
Stomach	Minimal mucosal inflammation(g).
Caecum	(Missing)
Skeletal muscle	(Missing)
Spinal cord	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver, Liver Perls', Spleen, Pancreas, Kidneys, Urinary bladder, Prostate, Seminal vesicles, Thyroids, Adrenals, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Colon, Eyes, Brain.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 4 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Focal subepithelial mononuclear cells.
Lungs	Moderate alveolar congestion/haemorrhage.
Lymph nodes	(Missing)
Spleen Perls'	Minimal Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells. Focus of basophilic cortical tubules.
Pituitary	(Missing)
Stomach	Minimal submucosal oedema(g).
Jejunum	(Missing)
Caecum	(Missing)
Colon	Parasite(s) in lumen.

The following tissues were considered normal:

Aorta, Heart, Liver, Liver Perls', Spleen, Pancreas, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Salivary gland, Oesophagus, Duodenum, Ileum, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 5 /M

Designated: . TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial mononuclear cells.
Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Foci of alveolar macrophages.
Lymph nodes	(Missing)
Liver	Minimal periportal mononuclear cells.
Spleen Perls'	Minimal Perls' positive material.
Kidneys	Occasional dilated tubules with eosinophilic contents.
Testes	Focus of interstitial cell hyperplasia.
Oesophagus	(Missing)
Caecum	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Spleen, Pancreas, Urinary bladder, Prostate, Seminal vesicles, Thyroids, Adrenals, Pituitary, Salivary gland, Stomach, Duodenum, Jejunum, Ileum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 6 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Moderate focal subepithelial mononuclear cells.
Lungs	Minimal pneumonitis. Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Spleen Perls'	Minimal Perls' positive material.
Pancreas	Minimal peri-islet siderocytes.
Urinary bladder	Parasite(s) in lumen.
Adrenals	Minimal focal medullary hyperplasia.
Pituitary	(Missing)
Oesophagus	(Missing)
Stomach	Minimal mucosal inflammation(g). Minimal submucosal oedema(g). Minimal submucosal inflammation(g).
Caecum	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Liver Perls', Spleen, Kidneys, Prostate, Seminal vesicles, Testes, Thyroids, Salivary gland, Duodenum, Jejunum, Ileum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 7 /M

Designated: TERMINAL

The following observations were noted:

Trachea	(Missing)
Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal pneumonitis. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells.
Lymph nodes	(Missing)
Liver	Focal bile duct proliferation. Area of mineralisation fibrosis and inflammation.
Spleen Perls'	Minimal Perls' positive material.
Pancreas	Focal exocrine acinar atrophy.
Urinary bladder	Parasite(s) in lumen.
Testes	(Missing)
Duodenum	(Missing)
Jejunum	(Missing)
Ileum	(Missing)
Caecum	(Missing)
Colon	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Spleen, Kidneys, Prostate, Seminal vesicles, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282
Level: 0 mg/kg/day
Rat No./Sex: R 10 /M
Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial lymphoid hyperplasia.
Lungs	Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Liver	Minimal foci of ground glass hepatocytes. Minimal foci of mononuclear cells.
Spleen Perls'	Minimal Perls' positive material.
Pancreas	Minimal periarteritis.
Kidneys	Minimal foci of interstitial mononuclear cells.
	Minimal foci of basophilic cortical tubules.
Oesophagus	(Missing)
Caecum	(Missing)
Colon	Minimal submucosal lymphoid hyperplasia.

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Spleen, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Salivary gland, Stomach, Duodenum, Jejunum, Ileum, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 11 /M

Designated: TERMINAL

The following observations were noted:

Lungs	Focal pneumonitis.
Lymph nodes	(Missing)
Liver	Minimal foci of mononuclear cells.
Spleen Perls'	Moderate Perls' positive material.
Urinary bladder	Parasite(s) in lumen. Parasites in mucosa.
Adrenals	Focus of cortical hyperplasia.
Duodenum	Minimal mucosal inflammation.
Jejunum	Minimal mucosal inflammation.
Ileum	Minimal mucosal inflammation.
Caecum	(Missing)
Colon	Minimal mucosal inflammation.
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver Perls', Spleen, Pancreas, Kidneys, Prostate, Seminal vesicles, Testes, Thyroids, Pituitary, Salivary gland, Oesophagus, Stomach, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 14 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation. Inflammatory cells in lumen.
Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal focal pneumonitis.
Lymph nodes	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Adrenals	Focal medullary hyperplasia.
Colon	Minimal submucosal lymphoid hyperplasia.

The following tissues were considered normal:

Aorta, Heart, Liver, Liver Perls', Spleen, Pancreas, Kidneys, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 16 /M

Designated: TERMINAL

The following observations were noted:

Lungs	Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Spleen Perls'	Trace of Perls' positive material.
Kidneys	Minimal foci of basophilic cortical tubules.
Urinary bladder	Parasite(s) in lumen.
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver, Liver Perls', Spleen, Pancreas, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 17 /M

Designated: TERMINAL

The following observations were noted:

Lungs	Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Liver	Minimal foci of ground glass hepatocytes.
Spleen Perls'	Moderate Perls' positive material.

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver Perls', Spleen, Pancreas, Kidneys, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 18 /M

Designated: TERMINAL

The following observations were noted:

Lungs	Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Marked focal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Liver	Minimal foci of mononuclear cells.
Spleen Perls'	Minimal Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver Perls', Spleen, Pancreas, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 22 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Minimal pneumonitis. Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Liver	Focal periportal fibrous tissue scarring. Minimal foci of siderocytes.
Spleen Perls'	Moderate Perls' positive material.
Stomach	Focal submucosal adipose tissue(g).
Jejunum	Submucosal lymphoid hyperplasia.
Caecum	Parasite(s) in lumen.
Skeletal muscle	(Missing)
Spinal cord	(Missing)
Brain	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Spleen, Pancreas, Kidneys, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum, Ileum, Colon, Eyes.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 24 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Moderate focal subepithelial inflammation.
Lungs	Minimal pneumonitis. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar lymphoid aggregates.
Liver	Minimal foci of hypertrophic hepatocytes. Area of fibrosis, inflammation and adipose tissue.
Spleen Perls'	Minimal Perls' positive material.
Duodenum	Minimal mucosal inflammation.
Jejunum	Minimal mucosal inflammation.
Ileum	Minimal mucosal inflammation.
Caecum	Minimal mucosal inflammation.
Colon	Minimal mucosal inflammation.
Skeletal muscle	(Missing)
Spinal cord	(Missing)
Brain	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Aorta, Heart, Lymph nodes, Liver Perls', Spleen, Pancreas, Kidneys, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Eyes.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 25 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal inflammatory cells in lumen.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal pneumonitis.
Lymph nodes	(Missing)
Liver	Minimal foci of mononuclear cells.
Spleen Perls'	Minimal Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.
	Minimal foci of basophilic cortical tubules. Cortical cyst.
Pituitary	(Missing)
Skeletal muscle	(Missing)
Spinal cord	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Spleen, Pancreas, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Eyes, Brain.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 26 /M

Designated: TERMINAL

The following observations were noted:

Aorta	(Missing)
Trachea	(Missing)
Heart	(Missing)
Lungs	(Missing)
Lymph nodes	(Missing)
Spleen Perls'	Minimal Perls' positive material.
Pancreas	(Missing)
Kidneys	Minimal foci of interstitial mononuclear cells. Focus of basophilic cortical tubules.
Urinary bladder	(Missing)
Prostate	(Missing)
Seminal vesicles	(Missing)
Testes	(Missing)
Thyroids	(Missing)
Adrenals	(Missing)
Pituitary	(Missing)
Salivary gland	(Missing)
Esophagus	(Missing)
Stomach	(Missing)
Duodenum	(Missing)
Jejunum	(Missing)
Ileum	(Missing)
Caecum	(Missing)
Colon	(Missing)
Skeletal muscle	(Missing)
Eyes	(Missing)
Spinal cord	(Missing)
Brain	(Missing)
Sternum	(Missing)

The following tissues were considered normal:
Liver, Liver Perls', Spleen.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 29 /M

Designated: TERMINAL

The following observations were noted:

Heart	Minimal foci of myocarditis.
Lungs	Minimal pneumonitis. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells.
Lymph nodes	(Missing)
Spleen Perls'	Minimal Perls' positive material.
Adrenals	Focal cortical hyperplasia.
Pituitary	Cyst(s) in pars anterior.
Duodenum	Minimal mucosal inflammation.
Skeletal muscle	(Missing)
Spinal cord	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Liver, Liver Perls', Spleen, Pancreas, Kidneys, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Salivary gland, Oesophagus, Stomach, Jejunum, Ileum, Caecum, Colon, Eyes, Brain.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 30 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Purulent bronchopneumonia.
Lymph nodes	(Missing)
Spleen Perls'	Minimal Perls' positive material.
Urinary bladder	Parasites in mucosa.
Salivary gland	Minimal foci of interstitial mononuclear cells.

The following tissues were considered normal:

Aorta, Heart, Liver, Liver Perls', Spleen, Pancreas, Kidneys, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 31 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Blood in lumen.
Lungs	Minimal peribronchiolar lymphoid aggregates. Moderate perivascular mononuclear cells.
Lymph nodes	(Missing)
Spleen	Minimal extramedullary haemopoiesis.
Spleen Perls'	Minimal Perls' positive material.
Pancreas	Minimal exocrine acinar atrophy.
Pituitary	Cyst(s) in pars anterior.
Stomach	Minimal submucosal inflammation(g).
Caecum	Parasite(s) in lumen. Minimal submucosal lymphoid hyperplasia.
Skeletal muscle	(Missing)
Spinal cord	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Liver Perls', Kidneys, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Colon, Eyes, Brain.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 32 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Blood in lumen.
Lungs	Minimal pneumonitis.
Spleen Perls'	Minimal Perls' positive material.
Kidneys	Minimal foci of basophilic cortical tubules.
Stomach	Minimal mucosal inflammation(g). Minimal submucosal inflammation(g).
Skeletal muscle	(Missing)
Spinal cord	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Aorta, Heart, Lymph nodes, Liver, Liver Perls', Spleen, Pancreas, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Caecum, Colon, Eyes, Brain.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 33 /M

Designated: TERMINAL

The following observations were noted:

Lungs	Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.
	Minimal foci of basophilic cortical tubules.
Pituitary	(Missing)
Stomach	Minimal submucosal inflammation(g).
Skeletal muscle	(Missing)
Spinal cord	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver, Liver Perls', Spleen, Pancreas, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Caecum, Colon, Eyes, Brain.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 37 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Moderate subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar acini with inflammation.
Lymph nodes	(Missing)
Liver	Minimal foci of ground glass hepatocytes.
Spleen Perls'	Minimal Perls' positive material.
Kidneys	Minimal foci of basophilic cortical tubules. Moderate foci of interstitial mononuclear cells.
Salivary gland	Moderate foci of interstitial mononuclear cells.

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Spleen, Pancreas, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 201 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Inflammatory cells in lumen. Subepithelial mononuclear cells.
Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal pneumonitis. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar acini with inflammation.
Lymph nodes	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Moderate foci of basophilic cortical tubules.
Urinary bladder	Parasite(s) in lumen. Minimal submucosal mononuclear cells.
Caecum	(Missing)
Spinal cord	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Liver Perls', Spleen, Pancreas, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Colon, Skeletal muscle, Eyes, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 204 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial mononuclear cells.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal pneumonitis. Minimal peribronchiolar acini with inflammation.
Lymph nodes	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Focus of basophilic cortical tubules.
Urinary bladder	Parasite(s) in lumen.
Stomach	Minimal mucosal inflammation(g). Minimal submucosal inflammation(g).
Caecum	(Missing)
Colon	Minimal submucosal inflammation.

The following tissues were considered normal:

Aorta, Heart, Liver, Liver Perls', Spleen, Pancreas, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 205 /M

Designated: TERMINAL

The following observations were noted:

Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Moderate peribronchiolar acini with inflammation. Moderate pneumonitis.
Lymph nodes	(Missing)
Spleen Perls'	Minimal Perls' positive material.
Seminal vesicles	Contracted.
Adrenals	(Missing)
Stomach	Minimal mucosal inflammation(g). Minimal submucosal inflammation(g).
Duodenum	Minimal mucosal inflammation.
Caecum	(Missing)
Colon	Minimal mucosal inflammation.

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver, Liver Perls', Spleen, Pancreas, Kidneys, Urinary bladder, Prostate, Testes, Thyroids, Pituitary, Salivary gland, Oesophagus, Jejunum, Ileum, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 210 /M

Designated: TERMINAL

The following observations were noted:

Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal pneumonitis. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar acini with inflammation.
Lymph nodes	(Missing)
Spleen Perls'	Minimal Perls' positive material.
Pituitary	(Missing)
Caecum	(Missing)
Spinal cord	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver, Liver Perls', Spleen, Pancreas, Kidneys, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Colon, Skeletal muscle, Eyes, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 211 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal focal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal pneumonitis. Minimal peribronchiolar acini with inflammation.
Lymph nodes	(Missing)
Liver	Minimal foci of mononuclear cells.
Spleen Perls'	Moderate Perls' positive material.
Pancreas	(Missing)
Kidneys	Minimal foci of interstitial mononuclear cells.
Testes	Minimal foci of interstitial cell hyperplasia.
Thyroids	Minimal focus of distended follicles.
Duodenum	Minimal mucosal inflammation.
Jejunum	Minimal mucosal inflammation.
Caecum	(Missing)
Spinal cord	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Spleen, Urinary bladder, Prostate, Seminal vesicles, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Ileum, Colon, Skeletal muscle, Eyes, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IPO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 212 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal pneumonitis. Minimal peribronchiolar acini with inflammation.
Lymph nodes	(Missing)
Liver	Minimal foci of mononuclear cells. Minimal foci of hypertrophic hepatocytes.
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.
Urinary bladder	Parasite(s) in lumen.
Testes	Minimal foci of interstitial cell hyperplasia.
Thyroids	Squamous cyst(s).
Adrenals	Focus of vacuolated cortical cells.
Stomach	Focus of submucosal adipose tissue(g).
Caecum	(Missing)
Colon	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Spleen, Pancreas, Prostate, Seminal vesicles, Pituitary, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 214 /M

Designated: TERMINAL

The following observations were noted:

Trachea	(Missing)
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Moderate peribronchiolar acini with inflammation. Purulent bronchopneumonia.
Liver	Minimal foci of basophilic hepatocytes.
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.
Jejunum	Minimal mucosal inflammation.
Ileum	Minimal mucosal inflammation.
Colon	Minimal mucosal inflammation.

The following tissues were considered normal:

Aorta, Heart, Lymph nodes, Liver Perls', Spleen, Pancreas, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Caecum, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 215 /M

Designated: TERMINAL

The following observations were noted:

Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal pneumonitis. Minimal foci of pigmented macrophages.
Lymph nodes	(Missing)
Spleen Perls'	(Missing)
Kidneys	Minimal foci of interstitial mononuclear cells. Minimal foci of basophilic cortical tubules. Foci of dilated cortical tubules with eosinophilic contents.
Caecum	(Missing)
Spinal cord	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver, Liver Perls', Spleen, Pancreas, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Colon, Skeletal muscle, Eyes, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 216 /M

Designated: TERMINAL

The following observations were noted:

Animal notes	Tumour bearing rat.
Trachea	Minimal subepithelial inflammation.
Lungs	Focal purulent bronchopneumonia. Minimal foci of mineralisation. Bronchiectasis.
Lymph nodes	(Missing)
Liver Perls'	Trace of Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal foci of dilated cortical tubules with eosinophilic contents.
Urinary bladder	Contains colloid.
Thyroids	Squamous cyst(s).
Pituitary	Adenoma of pars anterior [Neoplastic, Benign].
Ileum	(Missing)
Colon	Parasite(s) in lumen.

The following tissues were considered normal:

Aorta, Heart, Liver, Spleen, Pancreas, Prostate, Seminal vesicles, Testes, Adrenals, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Caecum, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 217 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Minimal pneumonitis. Focal alveolar haemorrhage. Bronchiolar haemorrhage. Moderate foci of pigmented macrophages.
Lymph nodes	(Missing)
Liver	Granuloma with central mineralisation.
Spleen Perls'	Minimal Perls' positive material.
Urinary bladder	Parasite(s) in lumen.
Stomach	Minimal submucosal inflammation(g).
Ileum	(Missing)
Colon	Minimal lymphoid hyperplasia.

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Spleen, Pancreas, Kidneys, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum, Jejunum, Caecum, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 219 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Minimal pneumonitis. Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Liver	Focus of ground glass hepatocytes.
Spleen Perls'	Minimal Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.
	Minimal foci of basophilic cortical tubules.
Colon	Minimal lymphoid hyperplasia.

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Spleen, Pancreas, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 220 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar acini with inflammation. Moderate foci of pigmented macrophages. Granuloma with central mineralisation. Pulmonary abscess(es).
Lymph nodes	(Missing)
Spleen Perls'	Minimal Perls' positive material.
Pancreas	Minimal focal exocrine acinar atrophy.
Pituitary	Prominent acini and ducts in pars nervosa.
Jejunum	(Missing)
Ileum	Minimal lymphoid hyperplasia.
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Liver Perls', Spleen, Kidneys, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Salivary gland, Oesophagus, Stomach, Duodenum, Caecum, Colon, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 221 /M

Designated: TERMINAL

The following observations were noted:

Trachea	(Missing)
Lungs	Minimal pneumonitis. Moderate foci of pigmented macrophages.
Lymph nodes	(Missing)
Liver	Minimal foci of mononuclear cells.
Spleen Perls'	Minimal Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.
Thyroids	(Missing)
Spinal cord	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Spleen, Pancreas, Urinary bladder, Prostate, Seminal vesicles, Testes, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 222 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Moderate peribronchiolar acini with inflammation. Minimal foci of pigmented macrophages. Bronchiectasis.
Lymph nodes	(Missing)
Liver	(Missing)
Liver Perls'	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Pancreas	Minimal focal inflammation.
Kidneys	Minimal foci of interstitial mononuclear cells. Minimal foci of basophilic cortical tubules.
Urinary bladder	Parasite(s) in lumen.
Pituitary	(Missing)
Colon	Parasite(s) in lumen.

The following tissues were considered normal:

Aorta, Heart, Spleen, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 223 /M

Designated: TERMINAL

The following observations were noted:

Aorta	(Missing)
Trachea	(Missing)
Heart	(Missing)
Lungs	Moderate peribronchiolar acini with inflammation. Minimal peribronchiolar lymphoid aggregates. Moderate pneumonitis. Minimal foci of pigmented macrophages.
Lymph nodes	(Missing)
Liver	Minimal foci of ground glass hepatocytes.
Liver Perls'	Minimal Perls' positive material.
Spleen	Minimal extramedullary haemopoiesis.
Spleen Perls'	Minimal Perls' positive material.
Pancreas	(Missing)
Kidneys	Minimal foci of interstitial mononuclear cells.
Urinary bladder	(Missing)
Prostate	(Missing)
Seminal vesicles	(Missing)
Testes	(Missing)
Thyroids	(Missing)
Adrenals	(Missing)
Pituitary	(Missing)
Salivary gland	(Missing)
Oesophagus	(Missing)
Stomach	(Missing)
Skeletal muscle	(Missing)
Eyes	(Missing)
Spinal cord	(Missing)
Brain	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Duodenum, Jejunum, Ileum, Caecum, Colon.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 226 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Moderate pneumonitis. Moderate foci of pigmented macrophages.
Lymph nodes	(Missing)
Liver	Minimal foci of hepatocyte vacuolation.
Spleen Perls'	Trace of Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.
Adrenals	Focus of vacuolated cortical cells.
Pituitary	(Missing)
Salivary gland	Minimal acini atrophy.
Ileum	Minimal mucosal inflammation.

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Spleen, Pancreas, Urinary bladder, Prostate, Seminal vesicles, Testes, Thyroids, Oesophagus, Stomach, Duodenum, Jejunum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 228 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Moderate subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Moderate pneumonia. Moderate foci of foamy macrophages.
Lymph nodes	(Missing)
Liver	Minimal foci of mononuclear cells.
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.
	Minimal foci of basophilic cortical tubules.
Thyroids	(Missing)
Pituitary	(Missing)
Stomach	Minimal submucosal inflammation(g).
Duodenum	(Missing)
Jejunum	(Missing)
Ileum	(Missing)
Caecum	(Missing)
Colon	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Spleen, Pancreas, Urinary bladder, Prostate, Seminal vesicles, Testes, Adrenals, Salivary gland, Oesophagus, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 229 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Moderate subepithelial inflammation. .
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal pneumonitis. Focus of pigmented macrophages.
Lymph nodes	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.
Testes	Minimal foci of interstitial cell hyperplasia.
Adrenals	Focus of cortical hyperplasia.
Eyes	Area of retinal atrophy.

The following tissues were considered normal:

Aorta, Heart, Liver, Liver Perls', Spleen, Pancreas, Urinary bladder, Prostate, Seminal vesicles, Thyroids, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 230 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Moderate subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar acini with inflammation. Moderate foci of foamy macrophages.
Lymph nodes	(Missing)
Liver	Focus of vacuolated hepatocytes.
Spleen Perls'	Minimal Perls' positive material.
Pancreas	Minimal focal exocrine acinar atrophy.
Kidneys	Minimal foci of interstitial mononuclear cells.
Urinary bladder	Minimal inflammation in mesentery.
	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Spleen, Prostate, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 231 /M

Designated: TERMINAL

The following observations were noted:

Aorta	(Missing)
Trachea	(Missing)
Heart	(Missing)
Lungs	(Missing)
Lymph nodes	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Pancreas	(Missing)
Kidneys	Moderate foci of interstitial mononuclear cells.
Urinary bladder	(Missing)
Prostate	(Missing)
Seminal vesicles	(Missing)
Testes	(Missing)
Thyroids	(Missing)
Adrenals	(Missing)
Pituitary	(Missing)
Salivary gland	(Missing)
Oesophagus	(Missing)
Stomach	(Missing)
Skeletal muscle	(Missing)
Eyes	(Missing)
Spinal cord	(Missing)
Brain	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Liver, Liver Perls', Spleen, Duodenum, Jejunum, Ileum, Caecum, Colon.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 235 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal pneumonitis. Marked peribronchiolar lymphoid aggregates. Foci of alveolar haemorrhage.
Lymph nodes	(Missing)
Spleen Perls'	Minimal Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.
Urinary bladder	Minimal serosal inflammation.
Testes	(Missing)
Stomach	Ectopic squamous epithelium(g).

The following tissues were considered normal:

Aorta, Heart, Liver, Liver Perls', Spleen, Pancreas, Prostate, Seminal vesicles, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 236 /M

Designated: TERMINAL

The following observations were noted:

Trachea	Moderate subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar acini with inflammation. Moderate foci of pigmented macrophages. Pulmonary abscess(es). Areas of foamy macrophages.
Lymph nodes	(Missing)
Liver	Minimal foci of hypertrophic hepatocytes.
Spleen	Minimal extramedullary haemopoiesis.
Spleen Perls'	Minimal Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.
Urinary bladder	Parasite(s) in lumen. Contains colloid.
Prostate	Focal prostatitis.
Stomach	Focal submucosal adipose tissue(g).
Skeletal muscle	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Pancreas, Seminal vesicles, Testes, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Caecum, Colon, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 243 /M

Designated: TERMINAL

The following observations were noted:

Aorta	(Missing)
Trachea	(Missing)
Heart	(Missing)
Lungs	(Missing)
Lymph nodes	(Missing)
Spleen Perls'	Minimal Perls' positive material.
Pancreas	(Missing)
Urinary bladder	(Missing)
Prostate	(Missing)
Seminal vesicles	(Missing)
Testes	(Missing)
Thyroids	(Missing)
Adrenals	(Missing)
Pituitary	(Missing)
Salivary gland	(Missing)
Oesophagus	(Missing)
Stomach	(Missing)
Ileum	(Missing)
Skeletal muscle	(Missing)
Eyes	(Missing)
Spinal cord	(Missing)
Brain	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Liver, Liver Perls', Spleen, Kidneys, Duodenum, Jejunum, Caecum, Colon.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 252 /F

Designated: TERMINAL

The following observations were noted:

Lungs	Minimal pneumonitis. Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Liver	Minimal foci of mononuclear cells.
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Caecum	(Missing)
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Spleen, Pancreas, Kidneys, Urinary bladder, Uterus, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Colon, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 253 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Moderate subepithelial inflammation.
Lungs	Minimal pneumonitis. Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal foci of dilated cortical tubules with eosinophilic contents.
Adrenals	Focus of vacuolated cortical cells.
Caecum	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Spleen, Pancreas, Urinary bladder, Uterus, Ovaries, Thyroids, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 254 /F

Designated: TERMINAL

The following observations were noted:

Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal pneumonitis. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal foci of pigmented macrophages.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Thyroids	Squamous cyst(s).
Caecum	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver, Spleen, Pancreas, Kidneys, Urinary bladder, Uterus, Ovaries, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 255 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Ovaries	Unilateral cyst(s).
Duodenum	(Missing)
Ileum	Minimal lymphoid hyperplasia.
Caecum	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Spleen, Pancreas, Kidneys, Urinary bladder, Uterus, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Jejunum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 256 /F

Designated: TERMINAL

The following observations were noted:

Lungs	Minimal pneumonitis. Minimal peribronchiolar lymphoid aggregates. Minimal foci of foamy macrophages.
Lymph nodes	(Missing)
Liver	Minimal foci of mononuclear cells.
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.
Pituitary	(Missing)
Caecum	(Missing)
Colon	Minimal lymphoid hyperplasia.
Brain	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Spleen, Pancreas, Urinary bladder, Uterus, Ovaries, Thyroids, Adrenals, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Skeletal muscle, Eyes, Spinal cord, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 258 /F

Designated: TERMINAL

The following observations were noted:

Lungs	Minimal pneumonitis. Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal foci of dilated cortical tubules with eosinophilic contents.
Urinary bladder	(Missing)
Caecum	(Missing)
Colon	Minimal lymphoid hyperplasia.

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver, Spleen, Pancreas, Uterus, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 259 /F

Designated: TERMINAL

The following observations were noted:

Lungs	Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Marked Perls' positive material.
Duodenum	(Missing)
Jejunum	(Missing)
Ileum	(Missing)
Caecum	(Missing)
Colon	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver, Spleen, Pancreas, Kidneys, Urinary bladder, Uterus, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 260 /F

Designated: TERMINAL

The following observations were noted:

Lungs	Minimal peribronchiolar lymphoid aggregates. Focal alveolar haemorrhage. Blood in bronchioles.
Lymph nodes	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal progressive glomerulonephrosis.
Ovaries	No corpora lutea.
Thyroids	Minimal distended follicles.
Pituitary	Focal hyperplasia in pars anterior.
Oesophagus	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver, Liver Perls', Spleen, Pancreas, Urinary bladder, Uterus, Adrenals, Salivary gland, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 262 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Moderate subepithelial inflammation.
Lungs	Marked peribronchiolar lymphoid aggregates. Bronchopneumonia.
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Marked Perls' positive material.
Uterus	Endometrial polyp.
Pituitary	Adjacent haemorrhage.
Colon	Minimal lymphoid hyperplasia.

The following tissues were considered normal:

Aorta, Heart, Lymph nodes, Liver, Spleen, Pancreas, Kidneys, Urinary bladder, Ovaries, Thyroids, Adrenals, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 264 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial lymphoid aggregates.
Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Pancreas	Minimal focal exocrine acinar atrophy.
Kidneys	Minimal progressive glomerulonephrosis.
Urinary bladder	Parasite(s) in lumen. Parasites in mucosa.
Ovaries	No corpora lutea. Follicular cysts.
Pituitary	(Missing)
Spinal cord	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Spleen, Uterus, Thyroids, Adrenals, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 265 /F

Designated: TERMINAL

The following observations were noted:

Animal notes	Tumour bearing rat.
Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Moderate peribronchiolar acini with inflammation. Bronchopneumonia.
Lymph nodes	(Missing)
Liver	(Missing)
Liver Perls'	(Missing)
Spleen Perls'	Marked Perls' positive material.
Ovaries	Bilateral cysts.
Pituitary	Adenoma of pars anterior [Neoplastic, Benign].
Stomach	Foci of submucosal adipose tissue(g).

The following tissues were considered normal:

Aorta, Heart, Spleen, Pancreas, Kidneys, Urinary bladder, Uterus, Thyroids, Adrenals, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 266 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Moderate subepithelial inflammation.
Lungs	Minimal pneumonitis. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal foci of dilated cortical tubules with eosinophilic contents.
Urinary bladder	Parasite(s) in lumen. Parasites in mucosa.
Uterus	Moderately dilated.
Stomach	Foci of submucosal adipose tissue(g).

The following tissues were considered normal:

Aorta, Heart, Liver, Spleen, Pancreas, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 268 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Moderate subepithelial inflammation.
Lungs	Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar lymphoid aggregates. Minimal peribronchiolar acini with inflammation. Bronchopneumonia.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Uterus	Minimal squamous metaplasia of endometrial glands.
Ovaries	No evidence of mass in section examined.

The following tissues were considered normal:

Aorta, Heart, Liver, Spleen, Pancreas, Kidneys, Urinary bladder, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 270 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar lymphoid aggregates. Minimal peribronchiolar acini with inflammation.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Pancreas	Minimal focal exocrine acinar atrophy.
Stomach	Foci of submucosal adipose tissue(g).
Caecum	Minimal lymphoid hyperplasia.
Colon	Parasite(s) in lumen.
Brain	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Spleen, Kidneys, Urinary bladder, Uterus, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Skeletal muscle, Eyes, Spinal cord, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 271 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate pneumonitis.
Lymph nodes	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Ovaries	No corpora lutea.
Eyes	Unilateral retinal atrophy.

The following tissues were considered normal:

Aorta, Heart, Liver, Liver Perls', Spleen, Pancreas, Kidneys, Urinary bladder, Uterus, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 272 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Moderate subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar acini with inflammation. Moderate pneumonitis.
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Stomach	Foci of submucosal adipose tissue(g).

The following tissues were considered normal:

Aorta, Heart, Lymph nodes, Liver, Spleen, Pancreas, Kidneys, Urinary bladder, Uterus, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 273 /F

Designated: TERMINAL

The following observations were noted:

Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal pneumonitis. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar acini with inflammation.
Liver Perls'	Minimal centrilobular Perls' positive material.
Spleen Perls'	Marked Perls' positive material.
Urinary bladder	Parasite(s) in lumen. Parasites in mucosa.
Ovaries	No corpora lutea.
Pituitary	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Lymph nodes, Liver, Spleen, Pancreas, Kidneys, Uterus, Thyroids, Adrenals, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 274 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal pneumonitis. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Uterus	Minimal squamous metaplasia of endometrial glands.
Ovaries	(Missing)
Spinal cord	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Spleen, Pancreas, Kidneys, Urinary bladder, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 275 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal pneumonitis. Minimal peribronchiolar acini with inflammation.
Lymph nodes	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Pancreas	Minimal focal exocrine acinar atrophy.
Duodenum	(Missing)
Jejunum	(Missing)
Ileum	(Missing)
Caecum	(Missing)
Colon	(Missing)
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Liver Perls', Spleen, Kidneys, Urinary bladder, Uterus, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 277 /F

Designated: TERMINAL

The following observations were noted:

Lungs	Pulmonary abscess(es). Bronchiectasis. Bronchopneumonia.
Lymph nodes	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Ovaries	No corpora lutea.
Colon	Parasite(s) in lumen.
Eyes	(Missing)
Spinal cord	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver, Liver Perls', Spleen, Pancreas, Kidneys, Urinary bladder, Uterus, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Skeletal muscle, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 278 /F

Designated: TERMINAL

The following observations were noted:

Aorta	(Missing)
Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen	Minimal extramedullary haemopoiesis.
Spleen Perls'	Moderate Perls' positive material.
Ovaries	(Missing)
Caecum	Minimal lymphoid hyperplasia.
Eyes	(Missing)
Brain	(Missing)

The following tissues were considered normal:

Trachea, Heart, Liver, Pancreas, Kidneys, Urinary bladder, Uterus, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Colon, Skeletal muscle, Spinal cord, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 279 /F

Designated: TERMINAL

The following observations were noted:

Aorta	(Missing)
Trachea	Moderate subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal pneumonitis. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells.
Lymph nodes	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Eyes	(Missing)
Spinal cord	(Missing)

The following tissues were considered normal:

Heart, Liver, Liver Perls', Spleen, Pancreas, Kidneys, Urinary bladder, Uterus, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 280 /F

Designated: TERMINAL

The following observations were noted:

Aorta	(Missing)
Trachea	(Missing)
Heart	(Missing)
Lungs	(Missing)
Lymph nodes	(Missing)
Liver	(Missing)
Spleen	(Missing)
Spleen Perls'	(Missing)
Pancreas	(Missing)
Kidneys	(Missing)
Urinary bladder	(Missing)
Uterus	(Missing)
Ovaries	(Missing)
Thyroids	(Missing)
Adrenals	(Missing)
Pituitary	(Missing)
Salivary gland	(Missing)
Oesophagus	(Missing)
Stomach	(Missing)
Duodenum	(Missing)
Jejunum	(Missing)
Ileum	(Missing)
Caecum	(Missing)
Colon	(Missing)
Skeletal muscle	(Missing)
Eyes	(Missing)
Spinal cord	(Missing)
Brain	(Missing)
Sternum	(Missing)

The following tissues were considered normal:
Liver Perls'.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 281 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal pneumonitis.
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal progressive glomerulonephrosis.
Urinary bladder	Parasite(s) in lumen.
Ovaries	Unilateral cyst(s).
Caecum	Parasite(s) in lumen.
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Heart, Lymph nodes, Liver, Liver Perls', Spleen, Pancreas, Uterus, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Colon, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 283 /F

Designated: TERMINAL

The following observations were noted:

Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Moderate pneumonitis.
Lymph nodes	(Missing)
Liver Perls'	Minimal centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Pancreas	(Missing)
Ovaries	No corpora lutea.
Caecum	(Missing)
Colon	Parasite(s) in lumen.
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver, Spleen, Kidneys, Urinary bladder, Uterus, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 284 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Minimal pneumonitis. Minimal peribronchiolar lymphoid aggregates.
'Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Marked Perls' positive material.
Pancreas	Focal exocrine acinar atrophy.
Urinary bladder	Parasite(s) in lumen. Parasites in mucosa.
Ovaries	Bilateral cysts.
Jejunum	Minimal lymphoid hyperplasia.
Caecum	Minimal lymphoid hyperplasia.
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Heart, Lymph nodes, Liver, Spleen, Kidneys, Uterus, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Ileum, Colon, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 285 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Moderate subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal pneumonitis. Minimal peribronchiolar acini with inflammation.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Ovaries	Cystic follicle(s).
Caecum	Parasite(s) in lumen. Minimal lymphoid hyperplasia.
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Spleen, Pancreas, Kidneys, Urinary bladder, Uterus, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Colon, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 286 /F

Designated: TERMINAL

The following observations were noted:

Trachea	(Missing)
Lungs	Minimal pneumonitis.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen	Minimal extramedullary haemopoiesis.
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.
Caecum	Minimal lymphoid hyperplasia.
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Pancreas, Urinary bladder, Uterus, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Colon, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 287 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal pneumonitis.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Pancreas	Minimal focal exocrine acinar atrophy.
Colon	Parasite(s) in lumen.
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Spleen, Kidneys, Urinary bladder, Uterus, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 288 /F

Designated: TERMINAL

The following observations were noted:

Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Moderate peribronchiolar acini with inflammation. Bronchopneumonia.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Stomach	Minimal mucosal inflammation(g).
Jejunum	Minimal lymphoid hyperplasia.
Ileum	Minimal lymphoid hyperplasia.
Colon	Parasite(s) in lumen.
Eyes	(Missing)
Spinal cord	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver, Spleen, Pancreas, Kidneys, Urinary bladder, Uterus, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum, Caecum, Skeletal muscle, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 289 /F

Designated: TERMINAL

The following observations were noted:

Lungs	Bronchiectasis.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Uterus	Minimal dilatation of endometrial glands.
Ovaries	No corpora lutea.
Stomach	Foci of submucosal adipose tissue(g).
Colon	Minimal lymphoid hyperplasia.
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver, Spleen, Pancreas, Kidneys, Urinary bladder, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Caecum, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 0 mg/kg/day

Rat No./Sex: R 290 /F

Designated: TERMINAL

The following observations were noted:

Aorta	(Missing)
Trachea	Minimal subepithelial inflammation.
Lungs	Minimal pneumonitis. Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Spleen Perls'	Marked Perls' positive material.
Kidneys	Minimal progressive glomerulonephrosis.
Ovaries	No corpora lutea.
Eyes	(Missing)

The following tissues were considered normal:

Heart, Liver, Liver Perls', Spleen, Pancreas, Urinary bladder, Uterus, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 451 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar acini with inflammation. Moderate pneumonitis. Moderate foci of pigmented macrophages.
Lymph nodes	(Missing)
Liver	(Missing)
Liver Perls'	(Missing)
Spleen	(Missing)
Spleen Perls'	(Missing)
Kidneys	Minimal foci of interstitial mononuclear cells.
Ovaries	No corpora lutea.
Adrenals	Minimal congestion.
Duodenum	(Missing)
Jejunum	(Missing)
Ileum	(Missing)
Caecum	(Missing)
Colon	(Missing)
Spinal cord	(Missing)

The following tissues were considered normal:

Aorta, Heart, Pancreas, Urinary bladder, Uterus, Thyroids, Pituitary, Salivary gland, Oesophagus, Stomach, Skeletal muscle, Eyes, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 453 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Minimal pneumonitis. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Liver	Minimal foci of mononuclear cells.
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Uterus	Minimal dilatation of lumen.
Ovaries	Unilateral parovarian cyst(s).
Caecum	(Missing)
Colon	Parasite(s) in lumen.

The following tissues were considered normal:

Aorta, Heart, Spleen, Pancreas, Kidneys, Urinary bladder, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 454 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Marked subepithelial inflammation. Squamous metaplasia of epithelium.
Lungs	Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Moderate peribronchiolar acini with inflammation. Bronchopneumonia.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Urinary bladder	Parasite(s) in lumen.
Stomach	Foci of submucosal adipose tissue(g).
Duodenum	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Spleen, Pancreas, Kidneys, Uterus, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 457 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Moderate peribronchiolar acini with inflammation. Minimal pneumonitis. Minimal foci of pigmented macrophages.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Pancreas	Focal exocrine acinar atrophy.
Stomach	Foci of submucosal adipose tissue(g).
Caecum	(Missing)
Colon	Minimal lymphoid hyperplasia.
Spinal cord	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Spleen, Kidneys, Urinary bladder, Uterus, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Skeletal muscle, Eyes, Brain.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 458 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Bronchiectasis. Bronchopneumonia.
Lymph nodes	(Missing)
Liver	Minimal foci of mononuclear cells.
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.
Adrenals	Minimal congestion. Minimal siderocytes.
Jejunum	(Missing)
Ileum	Minimal lymphoid hyperplasia.
Caecum	(Missing)

The following tissues were considered normal:

Aorta, Heart, Spleen, Pancreas, Urinary bladder, Uterus, Ovaries, Thyroids, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 459 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Liver	Minimal foci of mononuclear cells. Focal hepatocyte necrosis.
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.
Urinary bladder	Parasite(s) in lumen. Parasites in mucosa.
Adrenals	Focus of cortical hyperplasia.
Salivary gland	Minimal focal acinar atrophy.
Caecum	(Missing)

The following tissues were considered normal:

Aorta, Heart, Spleen, Pancreas, Uterus, Ovaries, Thyroids, Pituitary, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 460 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar acini with inflammation. Moderate pneumonitis.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen	Minimal extramedullary haemopoiesis.
Spleen Perls'	Moderate Perls' positive material.
Uterus	Minimal dilatation of lumen.
Ovaries	Bilateral inflammation.
Ileum	Minimal lymphoid hyperplasia. Fat necrosis in mesentery.
Caecum	Minimal lymphoid hyperplasia.

The following tissues were considered normal:

Aorta, Heart, Liver, Pancreas, Kidneys, Urinary bladder, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: . ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 461 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar lymphoid aggregates. Minimal peribronchiolar acini with inflammation. Moderate pneumonitis. Minimal foci of pigmented macrophages. Focus of foamy macrophages.
Lymph nodes	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Ovaries	Unilateral haemorrhagic cyst(s). Cyst(s).
Oesophagus	(Missing)
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Liver Perls', Spleen, Pancreas, Kidneys, Urinary bladder, Uterus, Thyroids, Adrenals, Pituitary, Salivary gland, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 462 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Minimal pneumonitis. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar lymphoid aggregates. Moderate foci of pigmented macrophages.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Uterus	Minimal dilatation of lumen.
Stomach	Foci of submucosal adipose tissue(g).
Ileum	(Missing)
Skeletal muscle	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Spleen, Pancreas, Kidneys, Urinary bladder, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum, Jejunum, Caecum, Colon, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 464 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal pneumonitis. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar acini with inflammation.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Pancreas	Minimal focal exocrine acinar atrophy.
Uterus	Minimal dilatation of endometrial glands.
Ovaries	No corpora lutea.
Caecum	Minimal lymphoid hyperplasia.

The following tissues were considered normal:

Aorta, Heart, Liver, Spleen, Kidneys, Urinary bladder, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 465 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Liver	Minimal vacuolated hepatocytes.
Spleen Perls'	Moderate Perls' positive material.
Pancreas	Minimal focal exocrine acinar atrophy.
Kidneys	Minimal progressive glomerulonephrosis.
Uterus	Minimal dilatation of lumen.
Ovaries	No corpora lutea.

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Spleen, Urinary bladder, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 466 /F

Designated: TERMINAL

The following observations were noted:

Animal notes	Tumour bearing rat.
Trachea	Moderate subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal pneumonitis. Minimal peribronchiolar acini with inflammation. Minimal foci of pigmented macrophages.
Lymph nodes	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Pancreas	(Missing)
Kidneys	Minimal foci of interstitial mononuclear cells. Minimal foci of dilated cortical tubules with eosinophilic contents.
Urinary bladder	Parasites in mucosa.
Pituitary	(Missing)
Spinal cord	(Missing)
Mammary gland	Mammary fibroadenoma [Neoplastic, Benign].

The following tissues were considered normal:

Aorta, Heart, Liver, Liver Perls', Spleen, Uterus, Ovaries, Thyroids, Adrenals, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 467 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal pneumonitis. Minimal peribronchiolar acini with inflammation. Moderate foci of pigmented macrophages.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Urinary bladder	Parasite(s) in lumen. Parasites in mucosa.
Uterus	Minimal dilatation of endometrial glands.
Caecum	Minimal lymphoid hyperplasia.
Colon	Parasite(s) in lumen.

The following tissues were considered normal:

Aorta, Heart, Liver, Spleen, Pancreas, Kidneys, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFC/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 468 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar acini with inflammation. Moderate pneumonitis. Moderate foci of pigmented macrophages.
Spleen Perls'	Trace of Perls' positive material.
Pancreas	Minimal focal exocrine acinar atrophy.
Urinary bladder	Parasites in mucosa.
Uterus	Minimal dilatation of lumen.
Adrenals	Focus of vacuolated cortical cells.

The following tissues were considered normal:

Aorta, Heart, Lymph nodes, Liver, Liver Perls', Spleen, Kidneys, Ovaries, Thyroids, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 470 /F

Designated: TERMINAL

The following observations were noted:

Animal notes	Tumour bearing rat.
Trachea	(Missing)
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal pneumonitis. Minimal foci of pigmented macrophages.
Lymph nodes	(Missing)
Liver	Minimal foci of mononuclear cells. Minimal vacuolated hepatocytes.
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal progressive glomerulonephrosis.
Pituitary	Adenoma of pars anterior [Neoplastic, Benign].
Stomach	Foci of submucosal adipose tissue(g). Minimal submucosal congestion(ng).
Caecum	Parasite(s) in lumen. Minimal lymphoid hyperplasia.

The following tissues were considered normal:

Aorta, Heart, Spleen, Pancreas, Urinary bladder, Uterus, Ovaries, Thyroids, Adrenals, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 471 /F

Designated: TERMINAL

The following observations were noted:

Lungs	Moderate peribronchiolar lymphoid aggregates. Minimal pneumonitis. Cyst not present in sections examined.
Lymph nodes	(Missing)
Liver	Focus of hypertrophic hepatocytes.
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Moderate foci of interstitial mononuclear cells.
Urinary bladder	(Missing)
Stomach	Foci of submucosal adipose tissue(g).
Caecum	Minimal lymphoid hyperplasia.
Colon	Minimal lymphoid hyperplasia.

The following tissues were considered normal:

Aorta, Trachea, Heart, Spleen, Pancreas, Uterus, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 472 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Minimal pneumonitis. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar lymphoid aggregates. Minimal peribronchiolar acini with inflammation. Moderate alveolar haemorrhage. Minimal alveolar oedema.
Lymph nodes	(Missing)
Liver	(Missing)
Liver Perls'	(Missing)
Spleen	(Missing)
Spleen Perls'	(Missing)
Pancreas	Minimal focal exocrine acinar atrophy.
Uterus	Moderate dilatation of lumen.
Ovaries	No corpora lutea.
Pituitary	(Missing)
Duodenum	(Missing)
Jejunum	(Missing)
Ileum	(Missing)
Caecum	(Missing)
Colon	(Missing)

The following tissues were considered normal:

Aorta, Heart, Kidneys, Urinary bladder, Thyroids, Adrenals, Salivary gland, Oesophagus, Stomach, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 473 /F

Designated: TERMINAL

The following observations were noted:

Trachea	(Missing)
Lungs	Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar lymphoid aggregates.
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal foci of interstitial mononuclear cells.
Ovaries	Cystic follicle(s).

The following tissues were considered normal:

Aorta, Heart, Lymph nodes, Liver, Spleen, Pancreas, Urinary bladder, Uterus, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Eyes, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 474 /F

Designated: TERMINAL

The following observations were noted:

Lungs	Minimal pneumonitis. Minimal peribronchiolar lymphoid aggregates. Moderate alveolar haemorrhage.
Lymph nodes	(Missing)
Liver	Minimal foci of mononuclear cells. Minimal bile duct hyperplasia. Early fibrous bridging.
Spleen Perls'	Moderate Perls' positive material.
Ovaries	No corpora lutea.
Stomach	Foci of submucosal adipose tissue(g).
Caecum	Minimal lymphoid hyperplasia.
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver Perls', Spleen, Pancreas, Kidneys, Urinary bladder, Uterus, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum; Jejunum, Ileum, Colon, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 477 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal pneumonitis.
Lymph nodes	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Duodenum	(Missing)
Jejunum	(Missing)
Ileum	(Missing)
Caecum	(Missing)
Colon	(Missing)
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Liver Perls', Spleen, Pancreas, Kidneys, Urinary bladder, Uterus, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 478 /F

Designated: TERMINAL

The following observations were noted:

Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal pneumonitis. Moderate foci of pigmented macrophages.
Lymph nodes	(Missing)
Liver	(Missing)
Liver Perls'	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Pancreas	Minimal focal exocrine acinar atrophy.
Stomach	Foci of submucosal adipose tissue(g).
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Spleen, Kidneys, Urinary bladder, Uterus, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 479 /F

Designated: TERMINAL

The following observations were noted:

Aorta	(Missing)
Trachea	(Missing)
Lungs	(Missing)
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Pancreas	(Missing)
Kidneys	Peripelvic lymphoid aggregates.
Urinary bladder	(Missing)
Uterus	(Missing)
Ovaries	(Missing)
Thyroids	(Missing)
Pituitary	(Missing)
Salivary gland	(Missing)
Oesophagus	(Missing)
Caecum	(Missing)
Skeletal muscle	(Missing)
Eyes	(Missing)
Spinal cord	(Missing)
Brain	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Heart, Liver, Spleen, Adrenals, Stomach, Duodenum, Jejunum, Ileum, Colon.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 480 /F

Designated: TERMINAL

The following observations were noted:

Aorta	(Missing)
Trachea	(Missing)
Lungs	(Missing)
Lymph nodes	(Missing)
Liver	(Missing)
Liver Perls'	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Pancreas	(Missing)
Kidneys	Focus of dilated cortical tubules with eosinophilic contents.
Urinary bladder	(Missing)
Uterus	(Missing)
Ovaries	(Missing)
Thyroids	(Missing)
Pituitary	(Missing)
Salivary gland	(Missing)
Oesophagus	(Missing)
Stomach	Foci of submucosal adipose tissue(g).
Caecum	Minimal lymphoid hyperplasia.
Skeletal muscle	(Missing)
Eyes	(Missing)
Spinal cord	(Missing)
Brain	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Heart, Spleen, Adrenals, Duodenum, Jejunum, Ileum, Colon.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 481 /F

Designated: TERMINAL

The following observations were noted:

Lungs	Minimal pneumonitis. Minimal peribronchiolar lymphoid aggregates. Moderate foci of pigmented macrophages.
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Pancreas	(Missing)
Urinary bladder	(Missing)
Stomach	Foci of submucosal adipose tissue(g).
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Trachea, Heart, Liver, Spleen, Kidneys, Uterus, Ovaries, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 483 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Moderate peribronchiolar lymphoid aggregates. Moderate bronchiolar epithelial hypertrophy with prominent goblet cells. Moderate peribronchiolar acini with inflammation. Minimal pneumonitis.
Lymph nodes	Abscess.
Liver	Minimal vacuolated hepatocytes.
Spleen Perls'	Marked Perls' positive material.
Ovaries	No corpora lutea.
Adrenals	Focus of vacuolated cortical cells.
Stomach	Foci of submucosal adipose tissue(g).
Eyes	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver Perls', Spleen, Pancreas, Kidneys, Urinary bladder, Uterus, Thyroids, Pituitary, Salivary gland, Oesophagus, Duodenum, Jejunum, Ileum, Caecum, Colon, Skeletal muscle, Spinal cord, Brain, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 484 /F

Designated: TERMINAL

The following observations were noted:

Aorta	(Missing)
Trachea	(Missing)
Lungs	Minimal peribronchiolar lymphoid aggregates. Minimal foci of pigmented macrophages. Foci of alveolar haemorrhage.
Lymph nodes	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Pancreas	(Missing)
Kidneys	Minimal foci of dilated cortical tubules with eosinophilic contents.
Urinary bladder	(Missing)
Uterus	(Missing)
Ovaries	(Missing)
Thyroids	(Missing)
Pituitary	(Missing)
Salivary gland	(Missing)
Oesophagus	(Missing)
Stomach	Foci of submucosal adipose tissue(g).
Colon	Minimal lymphoid hyperplasia.
Skeletal muscle	(Missing)
Eyes	(Missing)
Spinal cord	(Missing)
Brain	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Heart, Liver, Liver Perls', Spleen, Adrenals, Duodenum, Jejunum, Ileum, Caecum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 487 /F

Designated: TERMINAL

The following observations were noted:

Trachea	Minimal subepithelial inflammation.
Lungs	Minimal pneumonitis. Minimal bronchiolar epithelial hypertrophy with prominent goblet cells. Minimal peribronchiolar lymphoid aggregates.
Lymph nodes	(Missing)
Spleen Perls'	Moderate Perls' positive material.
Kidneys	Minimal foci of dilated cortical tubules with eosinophilic contents.
Ovaries	No corpora lutea.
Colon	Minimal lymphoid hyperplasia.
Eyes	(Missing)
Spinal cord	(Missing)
Brain	(Missing)

The following tissues were considered normal:

Aorta, Heart, Liver, Liver Perls', Spleen, Pancreas, Urinary bladder, Uterus, Thyroids, Adrenals, Pituitary, Salivary gland, Oesophagus, Stomach, Duodenum, Jejunum, Ileum, Caecum, Skeletal muscle, Sternum.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 489 /F

Designated: TERMINAL

The following observations were noted:

Aorta	(Missing)
Trachea	(Missing)
Lungs	(Missing)
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Marked Perls' positive material.
Pancreas	(Missing)
Kidneys	Minimal foci of interstitial mononuclear cells. Focus of dilated cortical tubules with eosinophilic contents.
Urinary bladder	(Missing)
Uterus	(Missing)
Ovaries	(Missing)
Thyroids	(Missing)
Pituitary	(Missing)
Salivary gland	(Missing)
Oesophagus	(Missing)
Skeletal muscle	(Missing)
Eyes	(Missing)
Spinal cord	(Missing)
Brain	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Heart, Liver, Spleen, Adrenals, Stomach, Duodenum, Jejunum, Ileum, Caecum, Colon.

Pathologist: L.E.Fish

Date: 24 Oct85

APPENDIX

(Pathology - continued)

IFO/26/27

Individual Animal Histopathology

Compound: ITF 282

Level: 85 mg/kg/day

Rat No./Sex: R 490 /F

Designated: TERMINAL

The following observations were noted:

Aorta	(Missing)
Trachea	(Missing)
Lungs	(Missing)
Lymph nodes	(Missing)
Liver Perls'	Trace of centrilobular Perls' positive material.
Spleen Perls'	Moderate Perls' positive material.
Pancreas	(Missing)
Urinary bladder	(Missing)
Uterus	(Missing)
Ovaries	(Missing)
Thyroids	(Missing)
Pituitary	(Missing)
Salivary gland	(Missing)
Oesophagus	(Missing)
Stomach	Foci of submucosal adipose tissue(g).
Caecum	Minimal mucosal inflammation. Minimal submucosal inflammation. Minimal submucosal oedema.
Colon	Minimal mucosal inflammation. Minimal submucosal inflammation.
Skeletal muscle	(Missing)
Eyes	(Missing)
Spinal cord	(Missing)
Brain	(Missing)
Sternum	(Missing)

The following tissues were considered normal:

Heart, Liver, Spleen, Kidneys, Adrenals, Duodenum, Jejunum, Ileum.

Pathologist: L.E.Fish

Date: 24 Oct85